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FIRST NAMED INVENTOR APPLICATION NO. FILING DATE ATTORNEY DOCKET NO. CONFIRMATION NO. 10/626,126 07/23/2003 9396 Timothy Lovenberg JJPR-0033/ORT-1377DIV2 23377 12/09/2005 EXAMINER 7590 WOODCOCK WASHBURN LLP LI, RUIXIANG ONE LIBERTY PLACE, 46TH FLOOR PAPER NUMBER ART UNIT 1650 MARKET STREET PHILADELPHIA, PA 19103 1646

DATE MAILED: 12/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

-	*	Application No.	Applicant(s)	
Office Action Summary		10/626,126	LOVENBERG ET AL.	
		Examiner	Art Unit	
		Ruixiang Li	1646	
The MAILING DATE of this communication appears on the cover sheet with the correspondence address Period for Reply				
A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION. - Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication. - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication. - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).				
Status				
1) 又	Responsive to communication(s) filed on 13 Oc	ctober 2005.		
·	· · · · · · · · · · · · · · · · · · ·	action is non-final.		
3)	Since this application is in condition for allowance except for formal matters, prosecution as to the merits is			
	closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11, 453 O.G. 213.			
Disposition of Claims				
4)🖂	Claim(s) <u>1-13 and 16</u> is/are pending in the application.			
	4a) Of the above claim(s) 12 and 13 is/are withdrawn from consideration.			
5)	Claim(s) is/are allowed.			
6)🛛	Claim(s) <u>1-3,5,8 and 11</u> is/are rejected.			
· <u> </u>	☑ Claim(s) <u>4,6,7,9,10 and 16</u> is/are objected to.			
8) Claim(s) are subject to restriction and/or election requirement.				
Applicati	on Papers			
9)⊠ The specification is objected to by the Examiner.				
10)⊠ The drawing(s) filed on <u>07/23/2003</u> is/are: a)⊠ accepted or b)□ objected to by the Examiner.				
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).				
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).				
11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.				
Priority under 35 U.S.C. § 119				
12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f). a) All b) Some * c) None of:				
1. Certified copies of the priority documents have been received.				
2. Certified copies of the priority documents have been received in Application No				
3. Copies of the certified copies of the priority documents have been received in this National Stage				
application from the International Bureau (PCT Rule 17.2(a)).				
* See the attached detailed Office action for a list of the certified copies not received.				
Attachment(s)				
1) Notic 2) Notic	e of References Cited (PTO-892) e of Draftsperson's Patent Drawing Review (PTO-948)	4)		
3) 🔯 Inform	nation Disclosure Statement(s) (PTO-1449 or PTO/SB/08) r No(s)/Mail Date 10/8/2004,6/9/2005, 4/11/2005.		atent Application (PTO-152)	

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DETAILED ACTION

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Election/Restrictions

1. Applicant's election of Group I, claims 1-10 and 16, in the reply filed on 10/13/2005 is

acknowledged. Because applicant did not distinctly and specifically point out the

supposed errors in the restriction requirement, the election has been treated as an

election without traverse (MPEP § 818.03(a)).

2. Applicants' preliminary amendment filed upon 07/23/2003 has been entered. Claims

1-13 and 16 are pending. Claims 1-11 and 16 are under consideration. Claims 12

and 13 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as

being drawn to a nonelected invention.

Drawings

3. The formal drawings filed on 07/23/2003 are accepted by the Examiner.

Information Disclosure Statement

4. The information disclosure statements submitted on 10/08/2004, 04/11/2005 and

06/09/2005 have been considered by the Examiner and a signed copy has been

attached to the office action.

Sequence Compliance

5. The amino acid sequence disclosure contained in this application does not comply

with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for

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the following reason(s): the amino acid sequences shown in Fig. 1 and 2 must be identified with a SEQ ID NO and an amendment directing its entry into the specification must be provided.

Objection to the Disclosure

- 6. The disclosure is objected to because of the following informalities:
- (i). A new title is required that is clearly indicative of the invention to which the claims are directed. The title is drawn to mammalian H4 receptors, but the claims are all drawn to mouse H4 receptors. The following title is suggested: DNA encoding mouse histamine receptor of the H4 subtype.
- (ii). The first paragraph of the specification fails to update the status of the parent application 09/790,849, now abandoned.
- (iii). The specification at page 11 discloses that the protein have a molecular weight of 44,495kDa, which appears to be an error.
- (iv). The Examples are not sequentially numbered.
- (v). The specification at page 39 refers to a PCR-generated sequence, depicted in Figure 6. However, Figure 6 is an amino acid sequence, which could not be directly generated by PCR.
- (vi). The title of the 2nd reference cited by applicant on page 53 is incorrect.

Claim Rejections—35 USC § 112, 1st paragraph

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-3 and 5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid encoding a polypeptide comprising SEQ ID NO: 9, does not reasonably provide enablement for an isolated nucleic acid recited in claim, part (b)-(d). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims.

The factors considered when determining whether a disclosure satisfies enablement requirement include: (i) the quantity of experimentation necessary; (ii) the amount of direction or guidance presented; (iii) the existence of working examples; (iv) the nature of the invention; (v) the state of the prior art; (vi) the relative skill of those in the art; (vii) the predictability or unpredictability of the art; and (viii) the breadth of the claims. *Ex Parte Forman*, 230 USPQ 546 (Bd Pat. App. & Int. 1986); *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

The invention is related to an isolated nucleic acid molecule that encodes rat histamine H4 receptor. Claim 1, part (c)-(d), is drawn to an isolated nucleic acid molecule comprising a nucleic acid molecule which is complementary to the polynucleotide of (a), comprising at least 15 sequential bases of the polynucleotide of (a), or hybridizes under stringent conditions to the polynucleotide of (a). Claims 2, 3, and 5 depend from claim 1. The claims does not require that the nucleic acid possess any particular conserved structure nor other disclosed distinguishing feature.

However, other than the cDNA sequences that encode histamine H4 receptors, the instant disclosure does not provide sufficient guidance and/or working examples regarding the structural and functional requirements commensurate in scope with what is encompassed by the instant claims. The disclosure does not show (i) which portions of the polypeptide of SEQ ID NO: 9 are critical to the activity of the polypeptide encoded by the nucleic acid of SEQ ID NO: 6; and (ii) what modifications (e.g., substitutions, deletions or additions) one can make to the polypeptide of SEQ ID NO: 9 will result in protein mutants with the same functions as that of the polypeptide of SEQ ID NO: 9. While teaching an isolated nucleic acid encoding a human histamine receptor (Behan et al., U.S. Patent No. 6,204,017, B1, March 20, 2001; 102(e) date: Oct. 7, 1999). The prior art does not teach how to make and use the genus of the nucleic acids that comprises at least 15 sequential bases of the nucleic acid encoding a protein comprising amino acids 1 to 389 of SEQ ID NO: 9. The state of the art (See, e.g., Ngo, et al, *The Protein Folding Problem and Tertiary* Structure Prediction, 1994, Merz, et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495) is such that the relationship between sequence of a protein and its activity is not well understood and is not predictable. Excising out portions of a protein or modifications to a protein, e.g., by substitutions or deletions, would often result in deleterious effects to the overall activity and effectiveness of the protein.

Moreover, claim 1 recites a functional limitation, "encodes a mammalian histamine H4 receptor protein", but part (b) and part (d) of claim 1 are drawn to a complementary sequence. It is well known in the art that if sequence X encodes

polypeptide Y, the complement of X will not encode polypeptide Y. Thus, the nucleic acids of claim 1, part (b) and (d) do not encode a histamine H4 receptor.

Therefore, the instant disclosure fails to enable the instantly claimed genus of nucleic acid molecules. It would require undue experimentation for one skilled in the art to make and use the claimed invention commensurate in scope with the claims.

9. Claims 1-3, 5, 8 and 11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

Claim 1, part (c), is drawn to an isolated nucleic acid molecule comprising at least 15 sequential bases of a nucleic acid molecule encoding a protein comprising amino acids 1 to 391 of SEQ ID NO: 9 or its complement. Claims 2 and 3 depend from claim 1. The claim does not require that the nucleic acid possess any particular conserved structure nor other disclosed distinguishing feature.

The instant disclosure of nucleic acid molecule of SEQ ID NO: 6 that encodes the polypeptide of SEQ ID NO: 9 does not adequately support the scope of the

claimed genus, which encompasses a substantial variety of subgenera including fulllength genes. A description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly & Co., 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant disclosure fails to provide sufficient description information, such as definitive structural or functional features of the claimed genus of nucleic acids. There is no description of the conserved regions that are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Furthermore, the prior art does not provide compensatory structural or correlative teachings to enable one skilled in the art to identify the encompassed nucleic acid molecules as being identical to those instantly claimed. Due to the breadth of the claimed genus and lack of the definitive structural or functional features of the claimed genus, one skilled in the art would not recognize from the disclosure that the applicant was in possession of the claimed genus.

Moreover, claims 5, 8, and 11 recite a genomic DNA. While specific cDNA sequences encoding histamine H4 receptors are disclosed, no genomic DNA sequences are disclosed. There is no description of the size of the genomic locus encoding the protein, nor is there even a mention of the numbers of introns and exons contained within the genomic sequence, let alone the disclosure of a complete

genomic sequence. There are no well-established rules, techniques, or procedures that would allow one of ordinary skill in the art to determine the genomic sequence given disclosed cDNA sequence. Thus, the claims to genomic DNAs do not meet the written description requirement.

Claim Rejections—35 USC § 102 (e)

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

- (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
- 11. Claims 1-3 and 5 are rejected under 35 U.S.C. 102(e) as being anticipated by Behan et al. (U.S. Patent No. 6,204,017, B1, March 20, 2001; 102(e) date: Oct. 7, 1999).

Behan et al. teach an isolated nucleic acid (SEQ ID NO: 1) that encodes a human histamine receptor and is 57.7% identical to SEQ ID NO: 6 of the present invention (see attached sequence alignment). The nucleic acid of Behan et al. comprises 25 sequential bases, i.e., nucleotides 131 to 156, of SEQ ID NO: 6 of the present invention. The complement of the nucleic acid taught by Behan et al. hybridizes under stringent conditions, by nature, to the nucleic acid sequence of SEQ ID NO: 6. Behan et al. also teach a nucleic acid fragment (column 7, lines 44-48) and its complement is complementary to, for example, nucleotides 131-156 of the nucleic

acid of SEQ ID NO: 6. Behan et al. further teach the nucleic acid can be an RNA or DNA (column 7, line 3), including genomic sequences (column 7, line 8). Accordingly, the reference of Behan et al. meets the limitations of claims 1 (b), (c), and (d), 2, 3, and 5.

Claim Objections—Minor Informalities

12. Claims 4, 6, 7, 9, 10, and 16 are objected to because of the following informalities: claims 4, 6, 7, 9, and 10 use an indefinite article to refer to a unique sequence; "a" or "an" should be amended to "the". Claim 16 depends from claim 6. Appropriate correction is required.

Conclusion

13. No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (571) 272-0829. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.

Ruixiang Li, Ph.D. Primary Examiner

December 6, 2005

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APPLICANT: Monsma, Frederick J. Jr.
APPLICANT: Walley L.
APPLICANT: Wall, Suke
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TITLE OF INVENTION: Histamine receptor
FILE REFERENCE: CN01069
CURRENT APPLICATION NUMBER: US/09/812,216
CURRENT FILING DATE: 2001-03-19
PRIOR APPLICATION NUMBER: 09/414,010
PRIOR APPLICATION NUMBER: 09/414,010
PRIOR PILING DATE: 1999-10-07
NUMBER OF SEQ ID NOS: 8
SOFTWARE: Patentin Ver. 2.1
SEQ ID NO 1
LENGTH: 1173
TYPE: DNA
ORGANISM: Homo sapiens
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GENERAL INFORMATION:
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APPLICANT: Hedrick, Joseph A.
APPLICANT: Laz, Thomas M.
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                                                                                                    CCATTGTGTCACAAGCGCTTTCAAAAGGCTTTCTTGAAAATATTTTGTATAAAAAAGCAA
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